

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
7 July 2005 (07.07.2005)

PCT

(10) International Publication Number  
**WO 2005/060973 A1**

(51) International Patent Classification<sup>7</sup>: **A61K 31/519**,  
A61P 35/00

Bengt [SE/SE]; Bergsbogatan 29, S-426 79 Västra  
Frölunda (SE). CARLSSON, Göran [SE/SE]; Vävarevä-  
gen 33, S-433 75 Jonsered (SE).

(21) International Application Number:  
PCT/SE2004/001955

(74) Agent: **AWAPATENT AB**; Box 11394, S-404 28 Göte-  
borg (SE).

(22) International Filing Date:  
22 December 2004 (22.12.2004)

(81) Designated States (*unless otherwise indicated, for every  
kind of national protection available*): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0303526-8 22 December 2003 (22.12.2003) SE

(71) Applicant (*for all designated States except US*): **BIOFOL**  
AB [SE/SE]; Bergsbogatan 29, S-426 79 Västra Frölunda  
(SE).

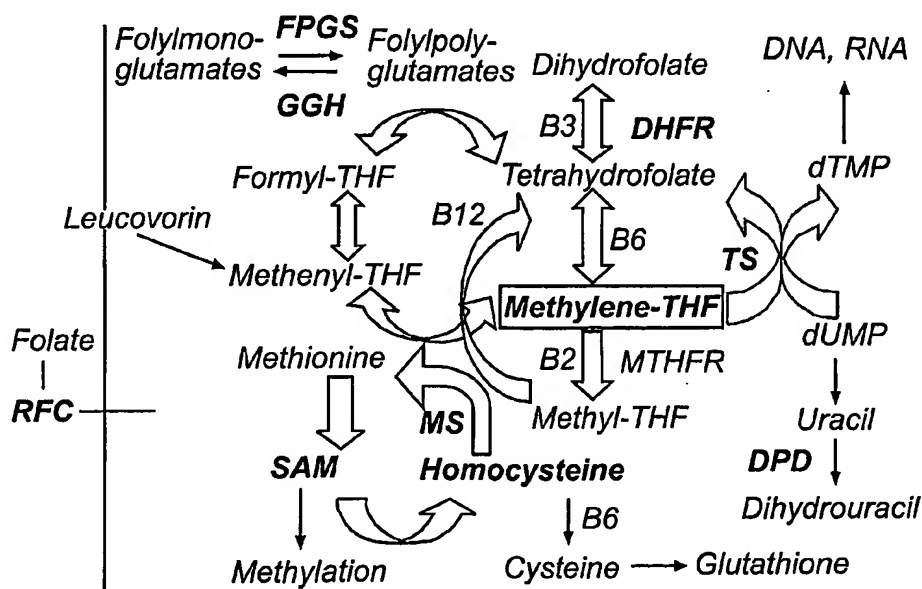
(84) Designated States (*unless otherwise indicated, for every  
kind of regional protection available*): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **GUSTAVSSON**,

[Continued on next page]

(54) Title: REDUCTION OF TOXICITY OF MULTI-TARGETING ANTIFOLATES



(57) Abstract: The use of tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate, and at least one multi-targeting antifolate, for the manufacture of a pharmaceutical composition for the treatment of cancer is disclosed. By combining the multi-targeting anti-folate with tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate, it is possible to remarkably reduce toxic side-effects without diminishing the anti-tumour action of the drugs. A pharmaceutical composition, a kit comprising the pharmaceutical composition as well as a method for the treatment of cancer are also disclosed.



SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declaration under Rule 4.17:**

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ,

NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

**Published:**

- with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.